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Spievack et al.

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[45] **Date of Patent: Feb. 16, 1999**

[54] **APPARATUS AND METHOD FOR ADMINISTERING A BIOLOGICALLY ACTIVE SUBSTANCE TO A BONE**

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[73] Assignee: **General Orthopedics**, Cambridge, Mass.

[21] Appl. No.: **556,230**

[22] Filed: **Nov. 9, 1995**

[51] **Int. Cl.**[6] **A61B 17/56**

[52] **U.S. Cl.** **606/60**; 606/73; 606/72; 606/65; 604/93; 604/890.1; 604/285

[58] **Field of Search** 606/62, 63, 65, 606/67, 72, 73, 86; 604/93, 890.1, 892.1, 285

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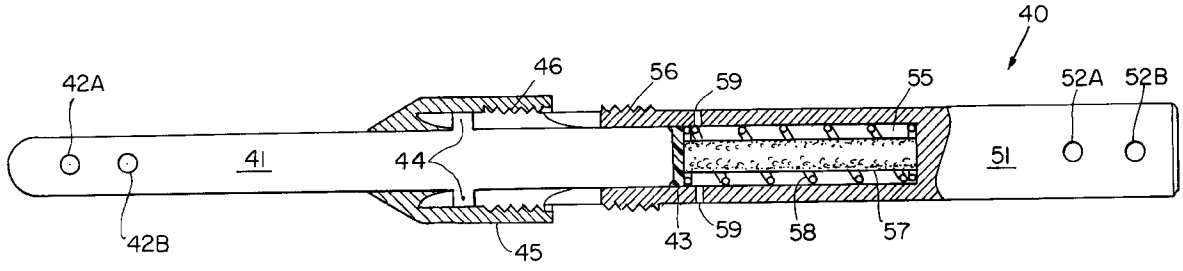
Assistant Examiner—Daphna Shai
Attorney, Agent, or Firm—Hamilton, Brook, Smith & Reynolds, P.C.

[57] **ABSTRACT**

A bone fastener is adapted to deliver biologically active substances to a bone site. An applicator is saturated with the substance and is disposed within an inner cavity of the fastener, near the bone site. Channels through the body of the fastener permit the substance to flow to the bone site. The substance can include therapeutic drugs, such as antibiotics, analgesics, bone morphogenic proteins, DNA, chemotherapy drugs and angiogenesis factors.

29 Claims, 6 Drawing Sheets



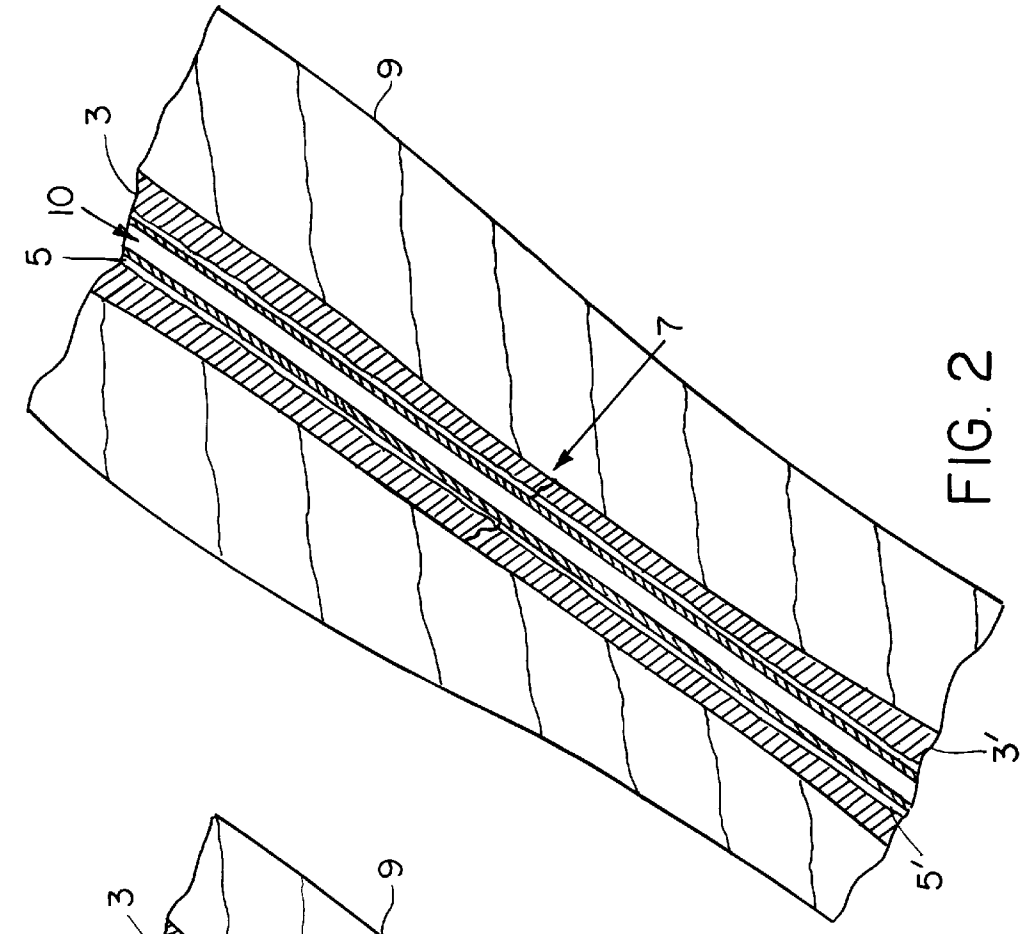


FIG. 2

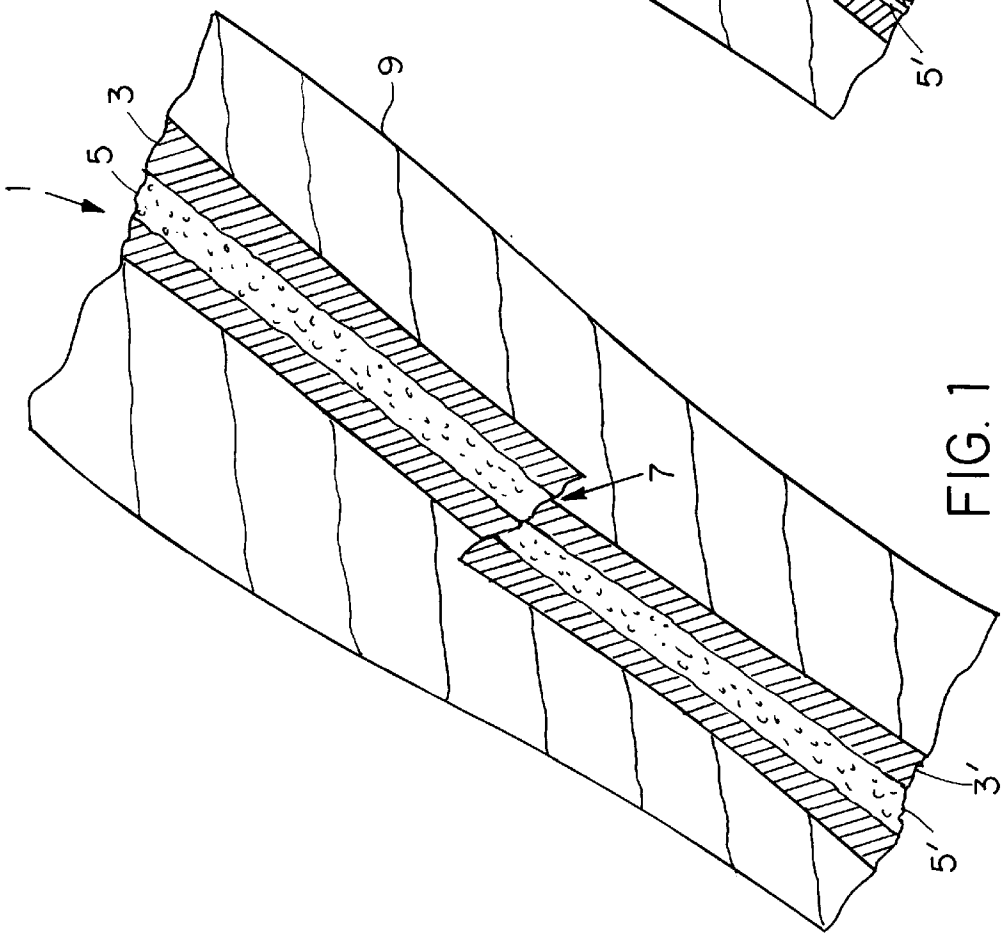


FIG. 1

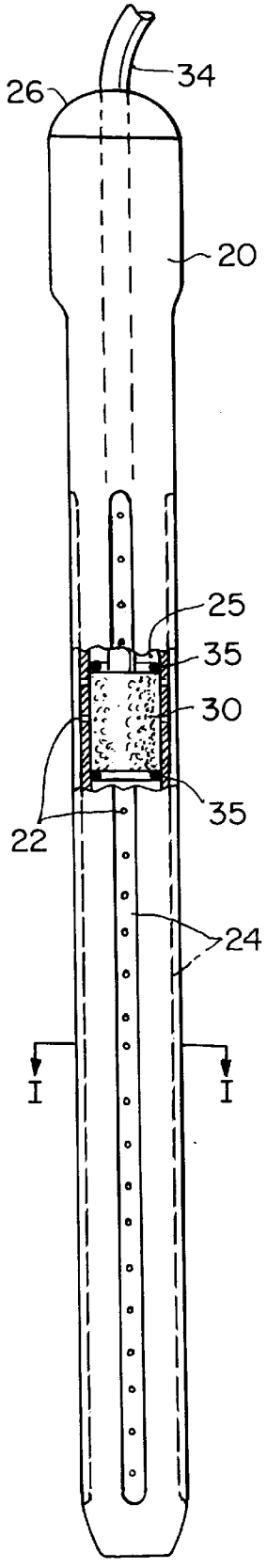


FIG. 3

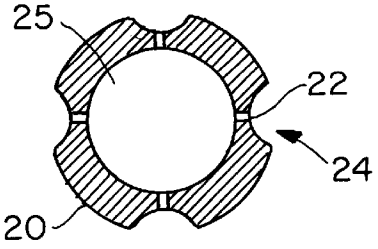


FIG. 4

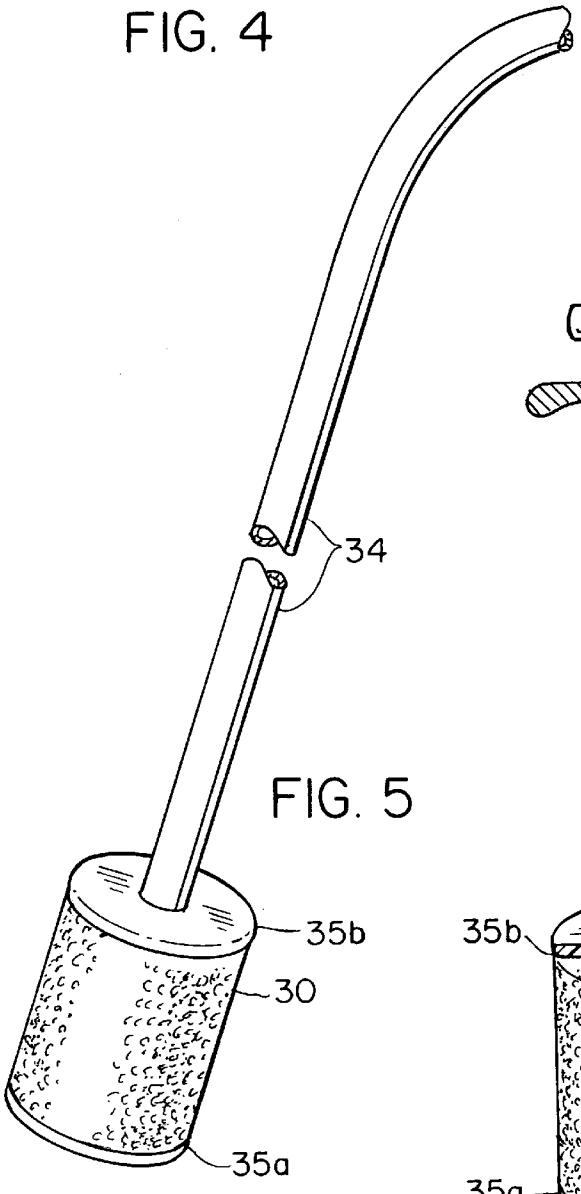


FIG. 5

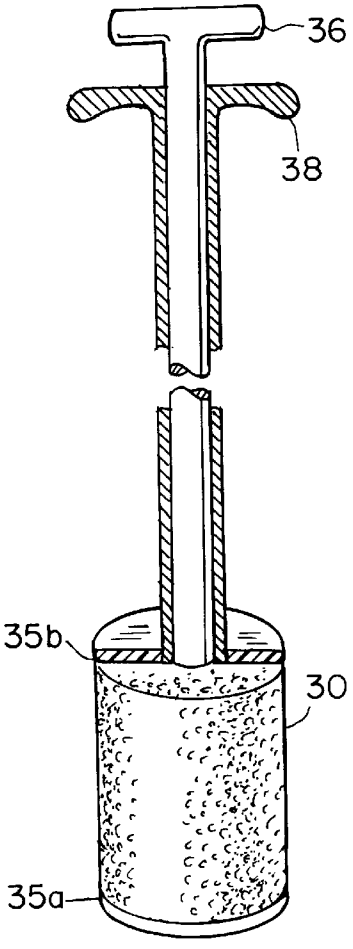
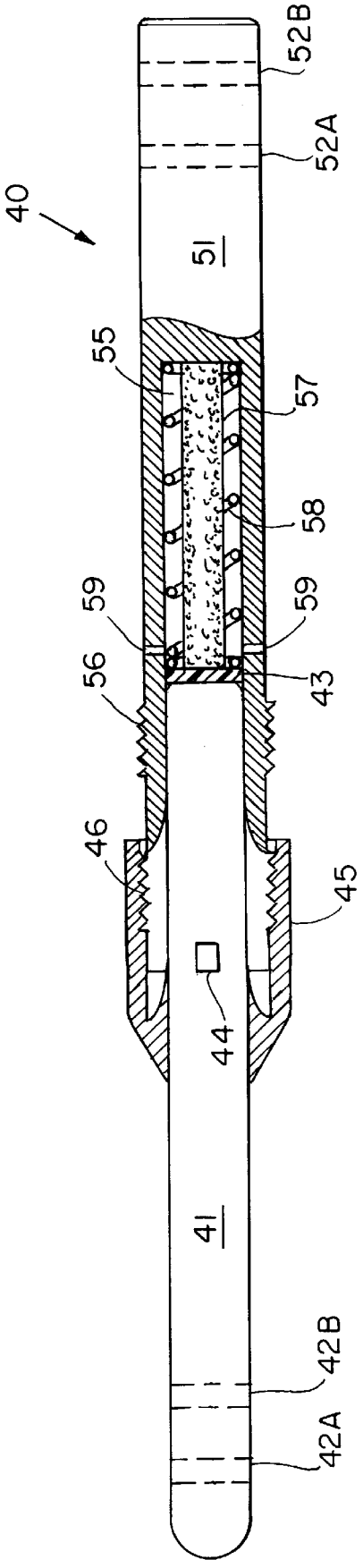


FIG. 6


40
51
52B
52A
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43
46
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44
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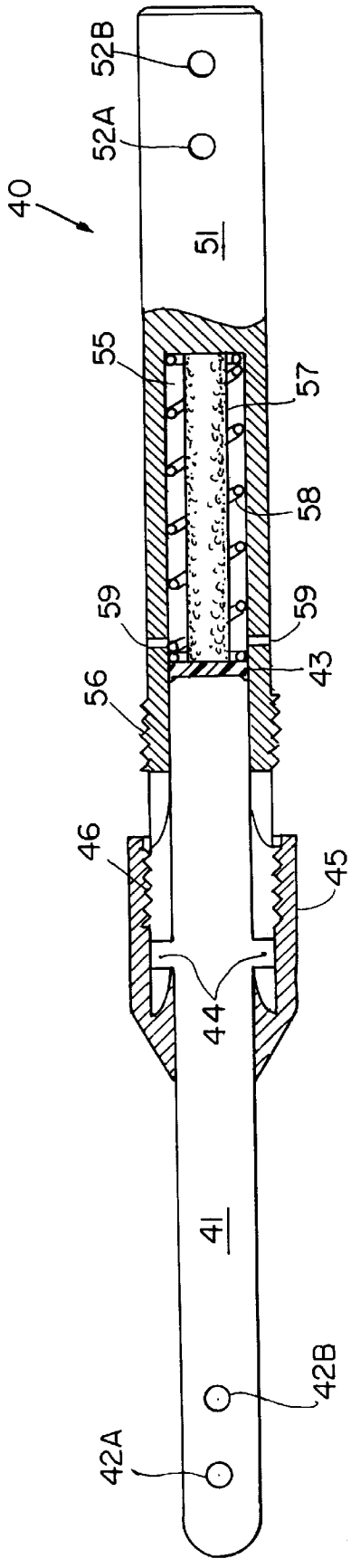
42B
42A

FIG. 7A


40
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52B
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FIG. 7B

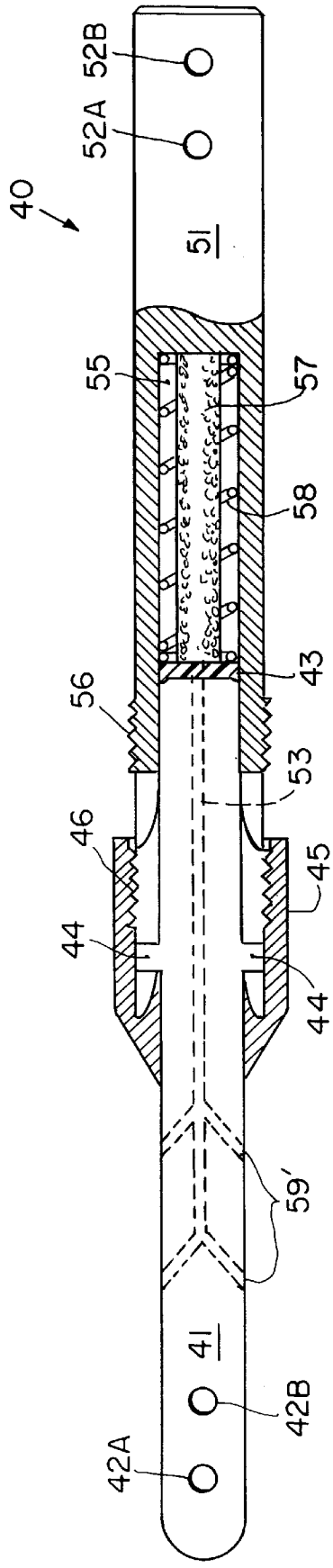

FIG. 7C

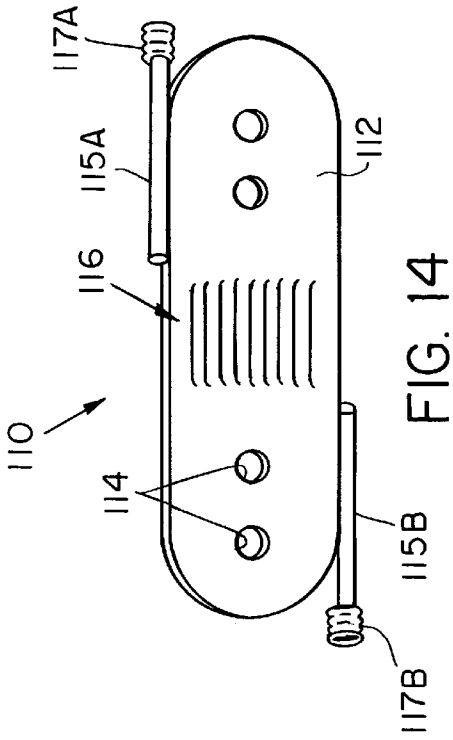

FIG. 14

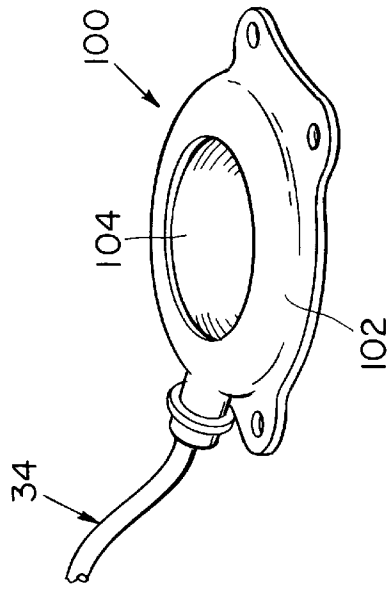

FIG. 13

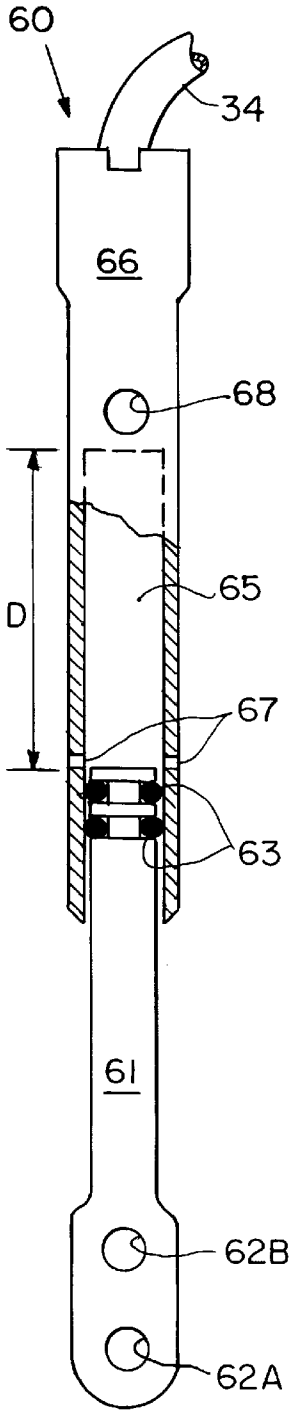

FIG. 8

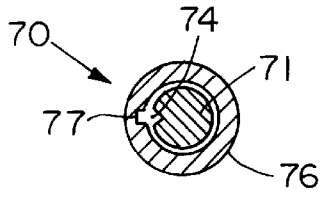

FIG. 10

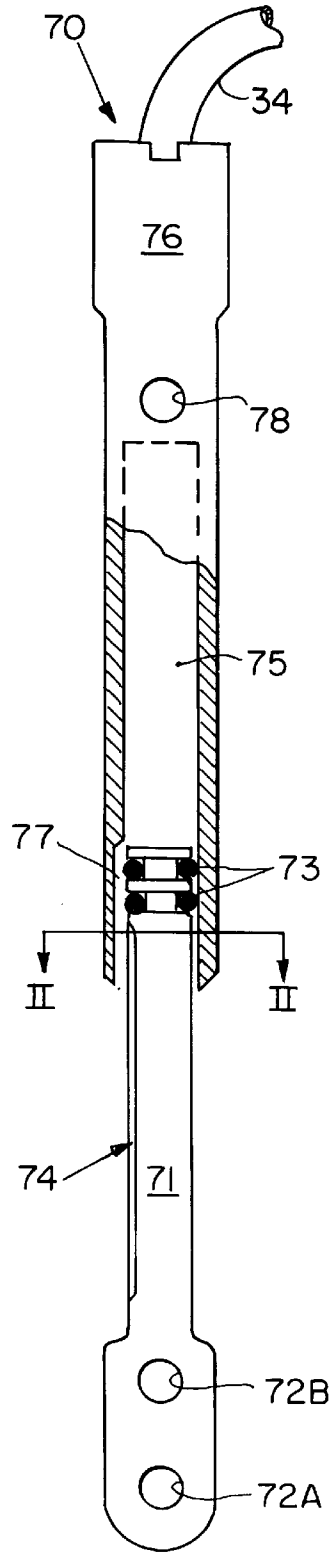

FIG. 9

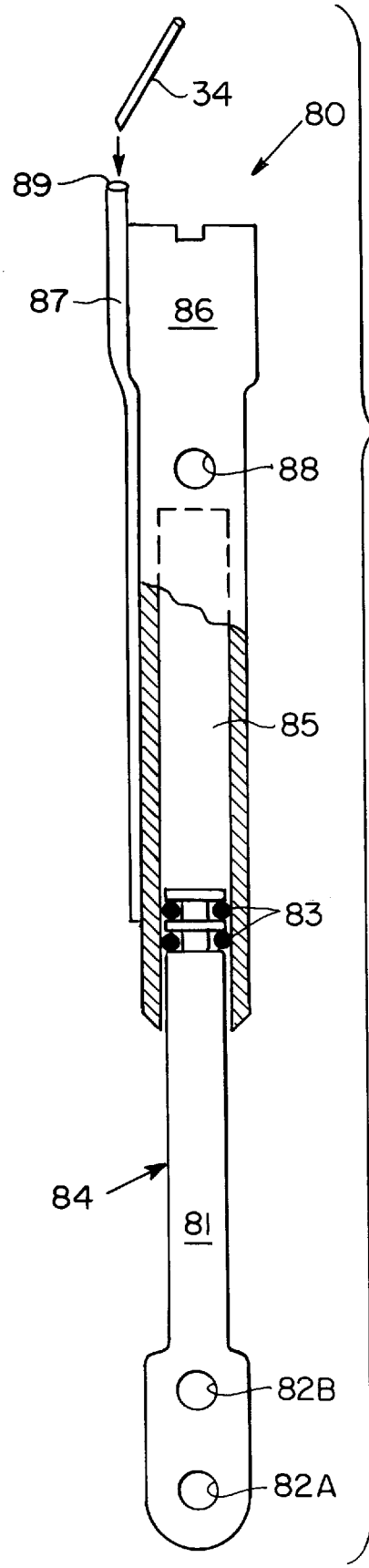

FIG. 11

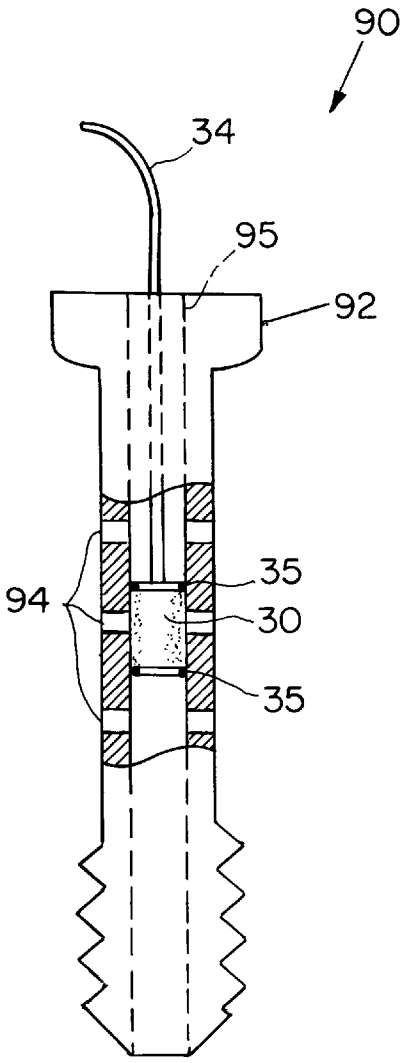

FIG. 12

APPARATUS AND METHOD FOR ADMINISTERING A BIOLOGICALLY ACTIVE SUBSTANCE TO A BONE

BACKGROUND OF THE INVENTION

Orthopedic fasteners have been used to repair bone fractures in the body of a human or other animal. For example, intramedullary nails are used to repair fractures in long bones of the body, such as the human femur. Intramedullary nails have also been used as a tool for lengthening femur bones, whereby the femur is surgically fractured and incrementally separated and allowed to regrow over time. In addition, reconstruction screws are used in hip reconstruction surgery and fracture plates are used for spine fractures.

In either case, an infection may occur at the fracture site or a bone growth factor may be required at the fracture site to stimulate bone growth. In those cases, further surgery may be required to deliver a therapeutic drug to the fracture site.

SUMMARY OF THE INVENTION

The invention solves or reduces the need for further invasive procedures by delivering biologically active substances, such as therapeutic drugs, to the fractured site of the bone through an implanted device. These therapeutic drugs include, but are not limited to, antibiotics, analgesics, bone morphogenic proteins, DNA, chemotherapy drugs and angiogenesis factors. Preferably, an intramedullary nail is used in a long bone of the body and is adapted to deliver the therapeutic drug. Besides fracture and osteotomy sites, the bone site can be a graft site. The invention, however, can be used to deliver therapeutic drugs to sites in other bones, such as hip bones or the spine, with a suitably adapted delivery structure, such as hip reconstruction screws or fracture plates. Similar devices can also be made in accordance with the invention to treat cartilage, such as in the knee.

In general, the invention relates to a device for administering a biologically active substance to a select bone site. The device includes a delivery structure which is implantable within, or attached to the surface of, a bone and is adapted to deliver the biologically active substance directly to the bone site. Preferably, the delivery structure is a bone fastener, such as an intramedullary nail, a reconstruction screw or a fracture plate.

A preferred embodiment of an intrabone fastener in accordance with the invention includes a fastener body which is adapted to be inserted into a selected bone. A cavity within the fastener body or a separate delivery structure stores the drug for delivery. There is at least one delivery channel extending from the cavity through the fastener body for delivering the therapeutic drug to the bone at a preselected bone site. Intrabone fasteners include intramedullary nails and reconstruction screws.

The cavity within the intrabone fastener can include an applicator or a collagen sponge saturated with the therapeutic drug. When the sponge is compressed by an external force, the drug is released from the sponge and flows through the delivery channels. In addition to a sponge or in conjunction therewith, a catheter can extend from the cavity of the fastener to the outside of the body or to an implanted reservoir accessibly via a needle so a physician can administer a dosage of the therapeutic drug to the bone site.

The foregoing and other objects, features and advantages of the invention, including various novel details of construction and combination of parts, will be apparent from the following more particular drawings and description of preferred embodiments of the apparatus and method for delivering a biologically active substance to a bone in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the invention. It will be understood that the particular bone fasteners embodying the invention are shown by way of illustration only and not as a limitation of the invention. The principles and features of this invention may be employed in varied and numerous embodiments without departing from the scope of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a foreshortened cross-sectional schematic diagram of a limb having a fractured bone.

FIG. **2** is a partial cross-sectional diagram of the fractured bone of FIG. **1** with an intramedullary nail fixed in place.

FIG. **3** is a schematic diagram, partially in cross-section, of a preferred embodiment of the invention embodied in an intramedullary nail.

FIG. **4** is a cross-sectional schematic diagram taken along line I—I of FIG. **3**.

FIG. **5** is a perspective view of an administering sponge system of FIG. **3**.

FIG. **6** is a perspective view of another embodiment of an administering sponge system for use with the intramedullary nail of FIG. **3**.

FIGS. **7A–7B** are schematic diagrams, partially in cross section, of a preferred embodiment of the invention embodied in a dynamized intramedullary nail.

FIG. **7C** is a schematic diagram, partially in cross section of another preferred embodiment of the invention embodied in a dynamized intramedullary nail.

FIG. **8** is a schematic diagram, partially in cross section, of a preferred embodiment of the invention embodied in a bone lengthening intramedullary nail.

FIG. **9** is a schematic diagram, partially in cross section, of another preferred embodiment of the invention embodied in a bone lengthening intramedullary nail.

FIG. **10** is a cross-sectional diagram taken along line II—II of FIG. **9**.

FIG. **11** is a schematic diagram, partially in cross section, of yet another preferred embodiment of the invention embodied in a bone lengthening intramedullary nail.

FIG. **12** is a cross-sectional schematic diagram of the invention embodied in an orthopedic screw.

FIG. **13** is a perspective view of an implantable reservoir for storing a biologically active substance in accordance with the invention.

FIG. **14** is a plan view of a preferred embodiment of the invention embodied in a fracture plate.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

FIG. **1** is a foreshortened cross-sectional schematic diagram of a limb **9** having a fractured bone **1**. Illustrated in the bone **1** are the bone cortex **3, 3'** and the intramedullary canal **5, 5'**. As illustrated, a fracture site **7** separates the bone **1** into two main sections: a proximal section nearer to the body and a distal section further from the body displaced from each other. The bone **1** can be repaired by reducing the fracture and fixing the two bone sections relative to each other with an orthopedic bone fastener.

FIG. **2** is a foreshortened cross-sectional schematic diagram of the fractured bone **1** of FIG. **1** having an intramed-

ullary nail **10** fixed in place. The bone sections are first aligned (i.e., reduced) and the intramedullary nail **10** is inserted. Over time, the fracture site **7** is healed by bone cell growth. Once healed, the intramedullary nail **10** may be removed from the bone **1**.

FIG. **3** is a schematic drawing, partially in cross-section, of a preferred embodiment of the invention embodied in an intramedullary nail. The nail has an elongate stainless steel body **20** with a hollow center cavity **25**. As illustrated, a columned pattern of via openings **22** extend through the nail body **20** to elongate grooves **24** on the exterior of the nail body **20**. The nail body **20**, delivery channels or vias **22** and flow channels or grooves **24** can be more readily appreciated from FIG. **4**.

FIG. **4** is a cross-sectional schematic diagram taken along line I—I of FIG. **3**. The intramedullary nail is fluted by the grooves **24**. Although the cross-section of the intramedullary nail is illustrated as being generally circular, other cross-sections can be employed in preferred embodiments of the invention. For example, the intramedullary nail can have a clover leaf cross-section and incorporate three columns of vias and grooves instead of the four columns shown.

Returning to FIG. **3**, a storage member in the form of an applicator such as a sponge **30** is illustrated in the internal cavity **25** of the nail body **20**. The sponge **30** is saturated with a biologically active substance which is later released into the bone through the vias **22** and down the grooves **24**. Preferably, the sponge **30** is placed at or near the selected bone site. Seals **35** are disposed at the top and bottom of the sponge **30** to contain the biologically active substance in the cavity **25**. A plurality of sponges can be placed in the intramedullary nail for treating numerous bone sites. Preferably the cross-section of the sponge **30** is adapted to match the cross-section of the cavity **25**.

The physician measures the distance along the nail to the fracture site using x-ray images or a fluoroscope and positions the sponge **30** near a bone site; absolute precision in positioning the sponge **30** is not required. As illustrated, a catheter **34** extends from the sponge **30** through the top of the nail to the outside of the body. A physician can administer additional biologically active substances to the sponge **30** through the catheter **34**. The top of the nail body **20** is sealed by a cannulated cap **26**.

FIG. **5** is a perspective view of the applicator system of FIG. **3**. The applicator system preferably includes a sponge **30** fabricated from collagen, for example. Illustrated is a bottom seal **35***a*, a top seal **35***b*, and the catheter **34**. Preferably, the catheter **34** is sufficiently rigid so that the physician can move the sponge **30** longitudinally within the intramedullary nail to position the sponge **30** near to the bone site **38** based on the known distance along the nail.

FIG. **6** is a perspective view of another embodiment of an administering sponge system for use in the intramedullary nail of FIG. **3**. A positioning handle **36** is connected to the bottom seal **35***a* and an activation handle **38** is connected to the top seal **35***b*. The positioning handle **36** is used by a physician to position the sponge near a selected bone site. Preferably, the sponge is saturated with the desired biologically active substance and the physician uses the activation handle **36** to squeeze the biologically active substance from the sponge. The activation handle **38** can operate as a pump to compress the sponge **30** between the seals **35***a*, **35***b* and lock into place or can activate a plunger which wrings out the sponge **30**. In response, the biologically active substance flows out of the vias **22** and down the grooves **24** in the nail body **20** to treat the bone site. After use, the sponge **30** can be removed from the intramedullary nail.

FIGS. **7A–7B** are schematic diagrams, partially in cross-section, of the invention embodied in a dynamized intramedullary nail **40**. The dynamized nail **40** includes a distal piston member **41** and a proximal cylinder member **51**. The piston member **41** includes two fixation holes **42A**, **42B** and the cylinder member **51** includes two fixation holes **52A**, **52B**. The piston member **41** is fabricated so that it can be received in a chamber or cavity **55** of the cylinder member **51**.

The piston member **41** and the cylinder member **51** are aligned by tabs **44** on the piston member **41**. The tabs **44** align with slots **53** on the cylinder member **51**. The assembly is locked together by a collar **45** having threads **46** which mate with threads **56** on the cylinder member **51**. When so aligned and secured by the collar **45**, the piston member **41** can move relative to the cylinder member **51** a distance determined by the length of the slots **53**.

To resist compression of the piston **41** into the cylinder member **51**, a spring member **58** is positioned within the cavity **55**. The spring member **58** resist compressive forces exerted by the piston **41** and returns the piston to the extended position after being compressed. Preferably, the piston stroke is about 0.25 mm because longitudinal motion of the bone with an amplitude of about 0.25 mm is known to stimulate bone growth. Although the spring member **58** is illustrated as a coiled spring, the spring member **58** can be an elastomer, flat spring or belville washer.

In a preferred embodiment of the invention, an applicator such as a sponge **57** is also disposed within the cavity **55**. The sponge **57** is saturated with a biologically active substance which, due to the compression of the spring member **58**, is forced out of vias **59** through the body of the cylinder member **51**. A seal **43** at the top of the piston member **41** creates an air seal around the cavity **55** and prevents the biologically active substance from seeping out through the joint between the piston member **41** and the cylinder member **51**.

FIG. **7C** is a schematic diagram, partially in cross section, of another preferred embodiment of the invention embodied in a dynamized intramedullary nail **40'**. Unlike the intramedullary nail **40** of FIGS. **7A–7B**, vias **59'** are formed in the piston member **41** instead of the cylinder member **51**. The vias **59'** are connected to the inner cavity **55** by a central cannulation **53**. Thus, when the spring member **58** is compressed, the biologically active substance is forced down the central cannulation **53** to the vias **59'**. In all other respects, the intramedullary nail **40'** of FIG. **7C** is identical to the intramedullary nail **40** of FIGS. **7A–7B**.

FIG. **8** is a schematic diagram, partially in cross-section, of a preferred embodiment of the invention embodied in a bone lengthening intramedullary nail **60**. Illustrated is a proximal cylinder member **66** having a fixation hole **68** and vias **67**. Vias **67** extend from the inner cavity **65** to the outer surface of the cylinder member **66**. Also illustrated is a distal piston member **61** which includes fixation holes **62A**, **62B** and seals **63**. In operation, the piston member **61** is extended outwardly from the cylinder member **66** by periodic finite amount until the bone is lengthened by a predetermined distance. Further details involving bone lengthening and suitable bone lengthening intramedullary nails are described by Alan Spievack in U.S. Pat. No. 5,350,379, the teachings of which are incorporated herein by reference.

Once the bone is extended to be the predetermined length, bone growth factors can be added to the osteotomy site to promote bone growth and hardening of the bone at the osteotomy site. In addition, once bone lengthening has stopped an antibiotic may need to be added to the bone site

to fight infections. As illustrated, the bone lengthening nail **60** has a maximum extension distance D defined by the top of the cavity **65** and the via openings **67**. The piston **61** is extended under hydraulic pressure through a catheter **34**. Traditionally, saline is used as the hydraulic fluid. Once the piston member **61** has extended the distance D, the saline flows out of the vias **67**. At that point, the biologically active substance can be added through the catheter **34**. The biologically active substance will also flow out the vias **67** to treat the nearby bone site.

FIG. **9** is a schematic diagram, partially in cross-section, of another preferred embodiment of the invention embodied in a bone lengthening intramedullary nail **70**. Like the intramedullary nail **60** of FIG. **8**, this bone lengthening nail **70** includes a piston member **71** having fixation holes **72**A, **72**B and a cylinder member **76** having a fixation hole **78**. A cavity **75** is formed within the cylinder member **76** and the piston member **71** moves longitudinally within the cavity **75**. Fluid is introduced by the catheter **34** and seals **73** on the piston member **71** prevent the fluid from escaping from the cavity **75**, thereby maintaining hydraulic pressure.

The intramedullary nail **70** includes a longitudinal delivery channel or slot **77** in the cylinder member **76** and a longitudinal flow channel or groove **74** in the piston member **71**. When the bone is fully lengthened and the piston member **71** is fully extended within the cylinder member **76**, fluid from the cavity **75** can flow out the slot **77** and down the groove **74**. In this way, the biologically active substance can be therapeutically applied to a bone site which interfaces with the groove **74** in the piston member **71**.

FIG. **10** is a cross-sectional diagram of the bone lengthening intramedullary nail **70** taken along line II—II of FIG. **9**. Illustrated is the piston member **71** within the cylinder member **76**. The groove **74** and the slot **77** are in alignment.

FIG. **11** is a schematic diagram, partially in cross section, of yet another preferred embodiment of the invention embodied in a bone lengthening intramedullary nail **80**. Like the intramedullary nails **60**, **70** of FIGS. **8** and **9**, this bone lengthening nail **80** includes a piston member **81** having fixation holes **82**A, **82**B and a cylinder member **86** having a fixation hole **88**. A cavity **85** is formed within the cylinder member **86** and the piston member **81** moves longitudinally within the cavity **85**. Seals **83** on the piston member **81** prevent fluid from escaping from the cavity **85**, thereby maintaining hydraulic pressure.

The intramedullary nail **80** includes a conduit **87** attached to the outside of the cylinder member **86**. A catheter **34** supplying a biologically active substance connects to the conduit **87** at a connector **89**. The biologically active substance from the catheter **34** flows down the conduit **87** to exit at a bone site.

The teachings of the invention can be applied to devices other than intramedullary nails. In particular, reconstruction screws for use in hip surgery can be modified according to the invention to deliver biologically active substances to a bone site within the hip.

FIG. **12** is a cross sectional schematic diagram of the invention embodied in an orthopedic screw **90**. The orthopedic screw **90** includes a screw body **92** as cannulated to form an inner cavity **95**. Vias **94** extend from the inner cavity **95** to the exterior of the screw body **92**. An administrating system, such as a sponge **30**, can be positioned relative to the vias **94** within the inner cavity **95**. As described above, the sponge **30** is positioned using a distance measurement obtained by an x-ray or fluoroscope machine. Once positioned, a biological active substance can be applied to the sponge **30** through a catheter **34**. The biologically active substance can then seep or be forced out through the vias **94** to a selected bone site. The sponge **30** can include top and bottom seals **35** to limit the dispersal of the biologically active substance to a particular region of the inner cavity **95**.

The above embodiments of the invention can use a catheter **34** for transmitting the biologically active substance to the bone site. The biologically active substance can be introduced to the catheter through an exterior port on the body or from an implantable reservoir.

FIG. **13** is a perspective view of an implantable reservoir for storing a biologically active substance in accordance with the invention. The reservoir **100** includes a reservoir body **102** which defines an inner storage volume and a silastic access port **104**. A physician can administer drugs to the reservoir **100** via a syringe and needle, with the needle penetrating the access port **104**. By applying pressure to the access port **104**, fluid from the reservoir **100** can also be forced through the catheter **34** under pressure. Such implantable reservoirs **100** can be obtained commercially from, for example, C. R. Bard.

Although the invention is well-suited to intrabone fasteners such as intramedullary nails and orthopedic screws, devices embodying the invention need not be positioned within a bone.

FIG. **14** is a plan view of a preferred embodiment of the invention embodied in a fracture plate. The fracture plate **110** includes a plate body **112** having fixation holes **114** therethrough. The fracture plate **110** is preferably used with fractures of the spine, wherein the fracture plate **110** is secured to the spine by the fixation holes **114**. The fracture plate **110** includes grooves **116** formed from a biologically absorbable material such as polyglycolic acid (PGA) laced with a biologically active substance. When the fracture plate **110** is positioned, the grooves **116** are placed in contact with a fracture site. Over time, the biologically absorbable material releases the biologically active substances at the bone site.

The fracture plate **110** can include optional conduits **115**A, **115**B for infusion of biologically active substances or drainage from the plate location. The conduits **115**A, **115**B are preferably fabricated from a metal, such as stainless steel, and bonded to the fracture plate **110** by welding or otherwise. Each conduit **115**A, **115** includes a connector **117**A, **117**B for coupling to a plastic infusion or drainage catheter. Preferably, one conduit **115**A is used for infusion and the other conduit **115**B is used for drainage, but both conduits **115**A, **115**B can be used for either infusion or drainage.

The dynamization technique can also be used with the fracture plate **110** to promote release of the biologically active substance from the grooves **116** or from other areas of the fracture plate **110**. For example, dynamization can be accomplished by enlarging one or more of the fixation holes **114** and encasing the fixation hole with the biologically active substance embedded in a delivery compound, such as PGA.

Equivalents

While this invention has been particularly shown and described with reference to preferred embodiment thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention as defined by the appended claims. For example, similar devices can also be made to treat cartilage in the knees or elsewhere.

These and all other equivalents are intended to be encompassed by the following claims.

The invention claimed is:

1. A device for administrating a biologically active therapeutic substance to a bone of a body having a treatment site requiring therapeutic treatment comprising:

a delivery structure implantable within a body;

a delivery mechanism having a dynamization mechanism and coupled to the delivery structure to deliver a therapeutic substance to a selected the treatment site of a bone in response to motion of the body; and

a replacement mechanism coupling the delivery structure to the outside of the body to facilitate replacement of the substance within the body.

2. The device of claim **1** wherein the delivery structure is a bone fastener having at least one channel through which the substance flows from inside the fastener to outside the fastener.

3. The device of claim **2** wherein the fastener is positionable so as to place a channel proximate to the treatment site of the bone.

4. The device of claim **1** wherein the delivery structure includes an internal cavity for storing the substance and at least one channel from the internal cavity to the exterior of the delivery structure.

5. The device of claim **4** further comprising a storage member disposed within the internal cavity to facilitate delivery of the substance over time.

6. The device of claim **5** wherein the replacement mechanism comprises a handle for withdrawal of the storage member from the body.

7. The device of claim **1** wherein the replacement mechanism comprises an infusion catheter extending from the delivery structure for providing a substance to the delivery structure under the control of a physician.

8. The device of claim **1** further comprising a drainage catheter extending from the delivery structure for draining fluid from the body.

9. The device of claim **1** wherein the delivery structure is implanted within the bone.

10. The device of claim **1** wherein the delivery structure is implanted adjacent to the bone.

11. An intramedullary nail for a bone having a medullary canal and a treatment site distally located along the medullary canal which requires therapeutic treatment comprising:

a fastener body shaped to be insertable through the medullary canal of a selected long bone of a body and to be extendable from a proximal entry point of the bone to a distal treatment site, the fastener body having a proximal fixation hole at a proximal end of the fastener body and a distal fixation hole at a distal end of the fastener body for securing the fastener body to the bone;

a cavity within the fastener body for storing a biologically active therapeutic substance; and

an administrating member within the cavity and between the proximal fixation hole and the distal fixation hole to facilitate delivery of the substance over time;

a replacement mechanism coupling the administrating member to the outside of the body to facilitate replacement of the substance within the body; and

at least one delivery channel extending from the cavity through the fastener body for delivering the substance from the administering member to the treatment site of the selected bone.

12. The intramedullary nail of claim **11** wherein the fastener body includes at least one flow channel on the exterior of the fastener body, each flow channel interfacing with at least one delivery channel to deliver the substance longitudinally along the fastener body.

13. The intramedullary nail of claim **11** wherein the administrating member is a sponge.

14. The intramedullary nail of claim **11** wherein the replacement mechanism comprises a catheter extending from the cavity for providing a substance to the cavity under the control of a physician.

15. The intramedullary nail of claim **11** further comprising a dynamization mechanism within the cavity to dynamize the fastener to urge deliver of the substance in response to motion of the body.

16. The intrabone fastener of claim **11** wherein the replacement mechanism comprises a handle for withdrawal of the administrative member from the body.

17. A method of fabricating an intramedullary nail for a bone having a medullary canal and a treatment site distally located along the medullary canal which requires therapeutic treatment, comprising the steps of:

forming a fastener body shaped to be insertable through the medullary canal of a selected long bone of a body and to be extendable from a proximal entry point of the bone to a distal treatment site;

forming a proximal fixation hole at a proximal end of the fastener body and a distal fixation hole at a distal end of the fastener body for securing the fastener body to the bone;

forming a cavity within the fastener body for storing a biologically active therapeutic substance;

disposing an administrating member within the cavity and between the proximal fixation hole and the distal fixation hole to facilitate delivery of the substance over time;

coupling a replacement mechanism between the administrative member and the outside of the body to facilitate replacement of the substance within the body; and

forming at least one delivery channel extending from the cavity through the fastener body for delivering the substance from the administrative number to the treatment site of the selected bone.

18. The method of claim **17** further comprising the steps of:

forming at least one flow channel on the exterior of the fastener body; and

interfacing each flow channel with at least one delivery channel to deliver the substance longitudinally along the fastener body.

19. The method of claim **17** wherein the administrating member is a sponge.

20. The method of claim **17** further comprising the step of disposing a spring member within the cavity to dynamize the fastener to urge deliver of the substance in response to motion of the body.

21. The method of claim **17** wherein the step of coupling comprises attaching an infusion catheter to the administrative member.

22. The method of claim **17** wherein the step of coupling comprises attaching a handle to the administrative member.

23. A device for administering a biologically active substance to a selected treatment site requiring therapeutic treatment within a body comprising:

a storage member for storing a biologically active therapeutic substance and being insertable within the body to a position proximate to the selected treatment site;

a replacement mechanism coupling the storage member to the outside of the body to facilitate replacement of the substance within the body; and

an extraction mechanism having a dynamization mechanism for extracting the biologically active substance from the storage member in response to motion of the body.

24. The device of claim **23** wherein the storage member is a sponge.

25. The device of claim **23** wherein the extraction mechanism is a compression device.

26. The device of claim **23** wherein the extraction mechanism is a wringing device.

27. The device of claim **23** wherein the replacement mechanism comprises an infusion catheter extending from the storage member for introduction of a biologically active substance to the storage member.

28. The device of claim **23** wherein the replacement mechanism comprises a handle for withdrawal of the storage member from the body.

29. The device of claim **23** wherein the treatment site is on a bone.

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